



A service of the National Library of Medicine
and the National Institutes of Health

My NCBI
[Sign In] [Regis]

All Databases PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Bool

Search PubMed for

Limits Preview/Index History Clipboard Details

Display AbstractPlus Show 20 Sort by Send to

All: 1 Review: 0

☐ 1: J Biol Chem. 2005 Apr 22;280(16):15700-8. Epub 2005 Feb 3.

Final Version FREE Links
J Biol Chem

Regulation and function of the sonic hedgehog signal transduction pathway in isolated gastric parietal cells.

Stepan V, Ramamoorthy S, Nitsche H, Zavros Y, Merchant JL, Todisco A.

Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor, Michigan 48109, USA.

Shh (Sonic hedgehog) regulates gastric epithelial cell differentiation. We reported that incubation of purified canine parietal cells with epidermal growth factor (EGF) for 6-16 h, stimulates H(+)/K(+)-ATPase alpha-subunit gene expression through the activation of Akt. We explored if Shh mediates some of the actions of EGF in the parietal cells. EGF induced a 6-fold increase in Shh expression, measured by Western blots, after 5 h of incubation. This effect was inhibited by both the phosphatidylinositol 3-kinase inhibitor LY294002 and by transduction of the cells with an adenoviral vector expressing dominant negative Akt. EGF stimulated the release of Shh-like immunoreactivity from the parietal cells, after 16 h of incubation. Shh induced H(+)/K(+)-ATPase alpha-subunit gene expression, assessed by Northern blots, it stimulated a luciferase reporter plasmid containing the EGF-responsive sequence (ERE) of the canine H(+)/K(+)-ATPase alpha-subunit gene promoter, and it induced parietal cell nuclear protein binding to the ERE. Gli transcription factors mediate the intracellular actions of Shh. Co-transfection of the parietal cells with the H(+)/K(+)-luc plasmid together with one expressing Gli2, induced H(+)/K(+)-luciferase activity 5-fold, whereas co-transfection of the cells with the H(+)/K(+)-luc plasmid together with one expressing dominant negative Gli2, inhibited EGF induction of H(+)/K(+)-luciferase activity. Identical results were observed in the presence of the Shh signal transduction pathway inhibitor, cyclopamine. Transfection of the cells with dominant negative Akt inhibited EGF, but not Shh stimulation of H(+)/K(+)-ATPase-luciferase activity. Thus, EGF but not Shh signals through Akt. Preincubation of the cells for 16 h with either Shh or EGF enhanced histamine-stimulated [(14)C]aminopyrine uptake by 50%. In conclusions, some of the actions of EGF in the parietal cells are mediated by the sequential activation of the Akt and the Shh signal transduction pathways. These effects

Related Links

Functional role of protein kinase B/Akt in gastric acid secretion. [J Biol Chem. 2001]

The Akt and MAPK signal-transduction pathways regulate growth factor actions in isolated gastric parietal cells. [Cell Centerology. 2004]

Extracellular signal-regulated protein kinases mediate H(+),K(+)-ATPase alpha-subunit gene expression. [Proc Natl Acad Sci USA. 2002]

Epidermal growth factor up-regulates expression of transforming growth factor beta receptor type II in human dermal fibroblasts by phosphoinositide 3-kinase/Akt signaling pathway: Resistance to epidermal growth factor stimulation in scleroderma fibroblasts. [Arch Biochem Biophys. 2003]

Requirement of BMP-2-induced phosphatidylinositol 3-kinase and Akt serine/threonine kinase in osteoblast differentiation and Smad-dependent BMP-2 gene transcription. [J Biol Chem. 2002]

See all Related Articles...

Exhibit 4

might represent novel mechanisms mediating the actions of growth factors on gastric epithelial cell differentiation.

PMID: 15691835 [PubMed - indexed for MEDLINE]

Display Show Sort by Send to

[Write to the Help Desk](#)

[NCBI](#) | [NLM](#) | [NIH](#)

[Department of Health & Human Services](#)

[Privacy Statement](#) | [Freedom of Information Act](#) | [Disclaimer](#)

Apr 30 2007 04:56:27